

### **REMARKS**

Claims 1-21 are currently pending. By this amendment, claims 4-6 and 10-21 have been canceled without prejudice to Applicant's reserve the right to pursue the subject matter of the canceled claims in one or more related applications. In addition, new claims 22-26 have been added and claims 1, 3, and 7 have been amended to clarify the subject matter of the present claims. Support for the amendments to claims 1, 3, and 7 and for new claims 23-26 may be found, *inter alia*, at p. 53, lines 19-22; p. 53 line 34 to p. 54, line 10; p. 58, lines 8-23; p. 99, line 33 to p. 100, line 20; p. 103, line 26 to p. 104, line 23; p. 105, lines 10-26; and p. 106, lines 1-9. Support for new claim 22 may be found at p. 98, lines 18-21; and p. 104, lines 13-14. As such, no new matter has been added. Therefore, claims 1-3, 7-9 and claims 22-26 will be pending upon entry of the instant amendment.

1. **THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN**

The Examiner has rejected claims 7-12 and 21 under 35 U.S.C. § 112, second paragraph, for failing to point out and distinctly claim the invention. The Examiner contends that claims 7 and 9 are allegedly indefinite for use of the phrase "polypeptide corresponds to."

Preliminarily, Applicants respectfully point out that claim 9 is dependent on claim 7 and that the phrase "polypeptide corresponds to" is found in claims 7 and 10. The Examiner contends that it is allegedly unclear whether a polypeptide "corresponding to" an amino acid sequence includes a polypeptide "comprising" said amino acid sequence or whether it allows a partial degree of correspondence, permitting some deviation in said amino acid sequence.

In response, applicant has amended claim 7 to recite that the polypeptide comprises the amino acid sequence SEQ ID NO:91 and has cancelled claim 10. Applicant submits that the amendment clarifies the meaning of claim 7, and its dependent claims, without narrowing its scope and, thus, obviates the instant rejection. Applicant therefore requests that the rejection under 35 U.S.C. § 112 be withdrawn.

2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION, SHOULD BE WITHDRAWN

A. *The Rejection As Drawn To Molecules That Interact With Skp2*

The Examiner has rejected claims 1, 3, 4, 6-11 under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The Examiner contends that

[t]he disclosure of Skp2 associating with Cks1 and binding to p27 does not adequately describe the wider genus of Skp-2 binding activity because p27 can be one of several different molecules targeted by Skp2 and there is no structural or functional nexus between p27 and other purported targets of Skp2...

In response, Applicant has amended claim 1 to recite that the test compound is contacted *in vitro* with a reaction mixture comprising Skp2, p27, Cdk2 and Cks1. As used in the specification, *e.g.*, Example 9, and, in particular at page 99, line 33 to page 100, line 3 and at page 104, lines 13-23, such a reaction mixture is a purified system containing known components. Further, the interaction Skp2 and each of the recited components has been extensively described in the specification. For example, the interaction of Skp2 with Cdk2 and/or p27 is described at page 93, line 33 to page 96, line 11; the interaction of Skp2 with Cks1 and p27 is described at p. 104, line 26 to p. 106, line 9. Accordingly, Applicant submits that the specification provides an adequate written description of Skp2 binding activity in the reaction mixture of the claimed methods and respectfully requests that the instant rejection be withdrawn.

B. *The Rejection as Drawn to Polypeptides Corresponding to SEQ ID NO:91*

The Examiner has rejected claims 7-12 under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The Examiner contends that claims 7-12 are reliant on a polypeptide “corresponding to” a polypeptide chain having the amino acid sequence SEQ ID NO:91, wherein such polypeptides can allegedly be read to have a only a degree of correspondence to SEQ ID NO:91. The Examiner further contends that claims 7 - 12 are thus reliant on a genus of polypeptides which differ in structure from SEQ ID NO:91.

As discussed above, claim 7 has been amended to recite that the polypeptide comprises SEQ ID NO:91. Applicants submit that the amendment clarifies that the polypeptide comprises the sequence SEQ ID NO:91 and respectfully requests that the rejection be withdrawn.

3. THE REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

A. *The Rejection Over Carrano As Evidenced By Ganoth*

The Examiner has rejected claims 1-9 under 35 U.S.C. § 103(a) as unpatentable over Carrano et al., 1999, Nature Cell Biology 1:193-199 (“Carrano”) as evidenced by Ganoth et al., 2001, Nature Cell Biol 3:321-324. Applicants believe that the amendments to claims 1-9 overcome the rejection for the reasons set forth below.

A finding of obviousness under 35 U.S.C. § 103(a) requires a determination that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O’Farrell*, 853 F.2d 894 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998). Further, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981 (CCPA 1974).

By investigating the interaction of Skp2 and p27, the present inventors have discovered and described the specific components necessary for the activity of the Skp2 complex *in vitro*. In particular, the instant application describes the a novel role for Cks1 in the interaction of Skp2 and p27. As taught in the specification, Cks1 is a critical component of any *in vitro* assay that seeks to measure this interaction. The claims, as amended herein, relate to an *in vitro* method of screening a test compound for modulation of Skp2 activity. Accordingly, the instantly claimed methods are directed to the *in vitro* use of a reaction mixtures that comprise the novel component of the Skp2 p27 interaction, Cks1.

In Carrano, the cellular machinery governing the ubiquitination and degradation of p27 in HeLa cells was investigated using immunoprecipitation and immunodepletion of HeLa cell extracts (see Carrano, FIGS. 1 and 2). In particular, Carrano identified that Skp2 specifically binds p27 and that cyclin E CDK2 was a necessary component of the cell extract in order to maintain and/or initiate p27 ubiquitination. However, Carrano does not provide any teachings or guidance as to the purified components of a reaction mixture for assaying

Skp2 binding activity or ubiquitin ligase activity, and particularly does not teach the required presence of Cks1 in such reaction mixtures. Thus, Carrano does not render obvious the presently claimed invention.

#### **4. REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING**

Claims 1-9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-22 of copending Application No. 10/632,150 ('150 application) in view of Carrano. The Examiner contends that the claims are not patentably distinct from each other because claims 20 and 22 of the '150 application in view of Carrano motivate one to detect the activity of Skp2 by measuring the ubiquitination of proteolysis of p27.

Claims 1-9 are further provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application Nos. 11/073,457 ('457 application); 11/073,460 ('460 application); 11/073,470 ('470 application) and 11/073,485 ('485 application). The Examiner contends that the claims are not patentably distinct from each other.

In response, Applicant believes that the amendments made herein overcome the obviousness-type double patenting rejection for the same reasons as discussed above; however, if appropriate, Applicant will consider submitting a Terminal Disclaimer once the claims are indicated to be allowable in the present application but for a Terminal Disclaimer. In the meantime, Applicants request that the double patenting rejections be held in abeyance.

### CONCLUSION

Entry of the foregoing amendments and remarks into the record of the above-identified application is respectfully requested. Withdrawal of all rejections and reconsideration of the amended claims is requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

No fee is believed due with the filing of this response. Should a fee be required, please charge any required fee to Jones Day Deposit Account No. 50-3013. A duplicate of this sheet is enclosed for accounting purposes.

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Respectfully submitted,

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